

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	5	"2005020825"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/12/08 14:06
L2	2	"20050020825"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/12/08 14:07
L3	2	"20050031588"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/12/08 14:09
L4	7	"2004002999"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/12/08 14:10
L5	6	"2004003000"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/12/08 14:40
L6	614	514/43.ccls.	US-PGPUB; USPAT	OR	ON	2006/12/08 14:40
L7	787	514/49.ccls.	US-PGPUB; USPAT	OR	ON	2006/12/08 14:40
L8	338	536/28.5.ccls.	US-PGPUB; USPAT	OR	ON	2006/12/08 14:40

10/607,909

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NEWS 4 AUG 28 ADISCTI Reloaded and Enhanced
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NEWS 6 SEP 11 CA/CAplus enhanced with more pre-1907 records
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NEWS 20 NOV 10 STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 21 NOV 13 CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 22 NOV 20 CAS Registry Number crossover limit increased to 300,000 in additional databases
NEWS 23 NOV 20 CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 24 NOV 20 CA/CAplus patent kind codes will be updated
NEWS 25 DEC 01 CAS REGISTRY enhanced with new classification scheme

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006

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10/607,909

FULL ESTIMATED COST

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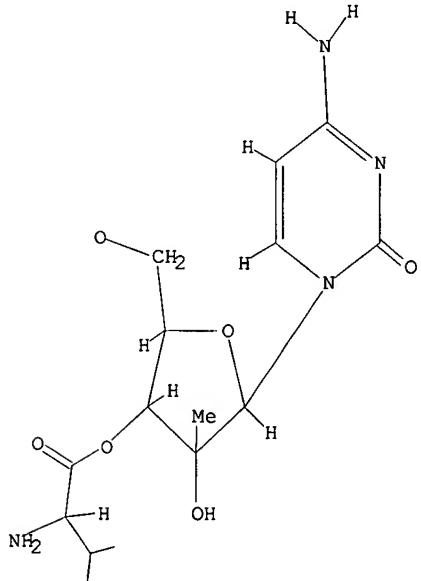
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experimental property data in the original document. For information
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<http://www.cas.org/ONLINE/UG/regprops.html>

=>
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L1 STRUCTURE uploaded

=> d 11
L1 HAS NO ANSWERS
L1 STR



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=> s 11 sss sam
SAMPLE SEARCH INITIATED 13:52:18 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 15 TO ITERATE

100.0% PROCESSED 15 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

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10/607,909

BATCH **COMPLETE**
PROJECTED ITERATIONS: 68 TO 532
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s 11 full
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FULL SCREEN SEARCH COMPLETED - 257 TO ITERATE

100.0% PROCESSED 257 ITERATIONS 30 ANSWERS
SEARCH TIME: 00.00.01

L3 30 SEA SSS FUL L1

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166.94 167.15

FILE 'CAPLUS' ENTERED AT 13:52:32 ON 08 DEC 2006
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=> s 13
L4 16 L3

=> d bib abs hitstr 1-16 14

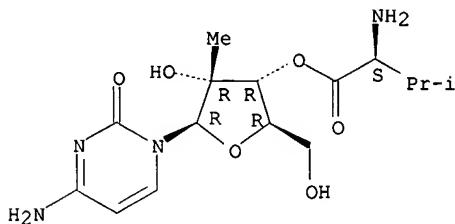
L4 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:1086375 CAPLUS
TI Ribavirin antagonizes the in vitro anti-hepatitis C virus activity of 2'-C-methylcytidine, the active component of valopicitabine
AU Coelmont, Lotte; Paeshuyse, Jan; Windisch, Marc P.; De Clercq, Erik; Bartenschlager, Ralf; Neyts, Johan
CS Rega Institute for Medical Research, KU Leuven, Louvain, 3000, Belg.
SO Antimicrobial Agents and Chemotherapy (2006), 50(10), 3444-3446
CODEN: AMACQO; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Ribavirin antagonizes the in vitro anti-hepatitis C virus (HCV) activity of the pyrimidine nucleoside analog 2'-C-methylcytidine, the active component of the exptl. anti-HCV drug valopicitabine. In contrast, the combination of ribavirin with either the purine nucleoside analog 2'-C-methyladenosine or the HCV protease inhibitor VX-950 resulted in an additive antiviral activity. These findings may have implications when planning clin. studies with valopicitabine.
IT INDEXING IN PROGRESS
IT 640281-90-9D, Valopicitabine, metabolite
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ribavirin antagonizes anti-hepatitis C virus activity of 2'-C-methylcytidine, active component of valopicitabine)
RN 640281-90-9 CAPLUS

McIntosh

10/607,909

CN L-Valine, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

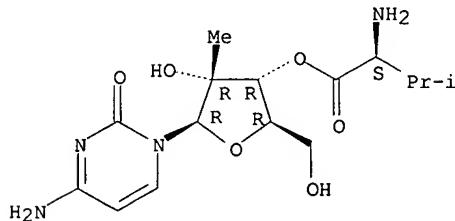
Absolute stereochemistry.



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

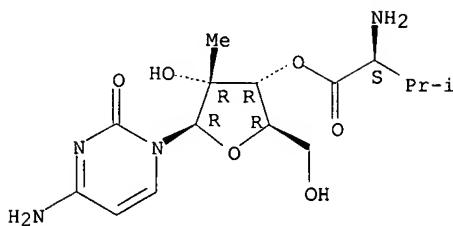
- L4 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:1011471 CAPLUS
DN 145:363620
TI Pharmaceutical compositions comprising ribofuranosylcytidine derivatives
IN Jores, Katja; Meyer, Andreas
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 14pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
- | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|----------|-----------------|----------|
| PI WO 2006100087 | A2 | 20060928 | WO 2006-EP2693 | 20060323 |
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CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM) | | | | |
| PRAI US 2005-664733P | P | 20050324 | | |
| AB | A pharmaceutical composition and granules are prepared by a wet granulation process. The pharmaceutical composition and granulates contain a therapeutic compound, e.g., the 3'-L-valine ester of β-D-2'-C-methylribofuranosylcytidine and its salts, esters, prodrugs or derivs. Tablets containing the above compound were prepared by wet granulation. | | | |
| IT | 640281-90-9 640725-71-9
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. comprising ribofuranosylcytidine derivs.) | | | |
| RN | 640281-90-9 CAPLUS | | | |
| CN | L-Valine, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME) | | | |

Absolute stereochemistry.



- RN 640725-71-9 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, dihydrochloride (9CI) (CA INDEX NAME)

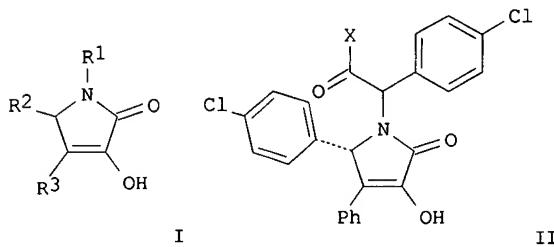
Absolute stereochemistry.



● 2 HCl

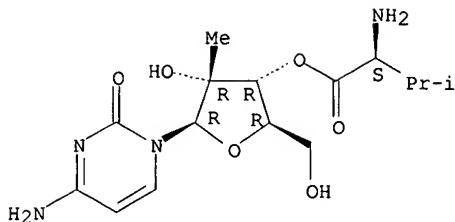
L4 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2006:981749 CAPLUS
 DN 145:335928
 TI Preparation of 1,5-dihydro-3-hydroxy-2H-pyrrol-2-ones as Mdm2 protein modulators
 IN Weber, Lutz
 PA Germany
 SO Ger. Offen., 11pp.
 CODEN: GWXXBX
 DT Patent
 LA German
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------------------|------|----------|----------------------|----------|
| PI DE 102005012681 | A1 | 20060921 | DE 2005-102005012681 | 20050318 |
| PRAI DE 2005-102005012681 | | 20050318 | | |
| OS MARPAT 145:335928 | | | | |
| GI | | | | |



AB Title compds. I [R1, R2 = cycloalkyl, heteroaryl, aryl, etc.; R3 = H, alkyl, cycloalkyl, etc.] and their pharmaceutically acceptable salts were prepared. For example, coupling of carboxylic acid II [X = OH] and 2-methoxyethylamine afforded amide II [X = NHCH2CH2OCH3]. Compds. I are noted as Mdm2 protein modulators (no data provided).
 IT 640281-90-9, Valopicitabine
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (medicaments with; preparation of 3-hydroxy-2H-pyrrolones as Mdm2 protein modulators)
 RN 640281-90-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2006:976176 CAPLUS
 DN 145:335951

TI Tetrahydroisoquinolin-1-ones as HDM2 ligands, their preparation, pharmaceutical compositions, and use for the treatment of cancer

IN Weber, Lutz

PA Germany

SO PCT Int. Appl., 42pp.
 CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| PI WO 2006097323 | A1 | 20060921 | WO 2006-EP2471 | 20060317 |
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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM | | | | |

PRAI DE 2005-102005012680 A 20050318

OS MARPAT 145:335951

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to compds. according to formula I, which are HDM2 protein ligands, inducing apoptosis and inhibiting proliferation, and having therapeutic utility in cancer therapy. In compds. I, R1 is selected from (un)substituted morpholinyl, (un)substituted pyrrolidinyl, (un)substituted piperazinyl, OR5, and NR5R6, where R5 and R6 are independently selected from H, alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl; R2 and R3 are independently selected from aryl, heteroaryl, arylalkyl, or heteroarylalkyl; and R4 is selected from H, OH, halo, nitro, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, and NR7R8, where R7 and R8 are independently selected from H, lower alkyl, lower alkoxyalkyl, heterocyclyl, aryl, and heteroaryl. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I, optionally in combination with a pharmaceutically acceptable carrier, as well as to the use of the compns. for the treatment of cancer. Condensation of 4-chlorobenzaldehyde with 4-chlorobenzylamine followed by heterocyclization with homophthalic anhydride gave isoquinolinonecarboxylic acid II, which was amidated with 2-methoxyethylamine to give isoquinolinone III. The compds. of the invention are ligands of HDM2 (no data).

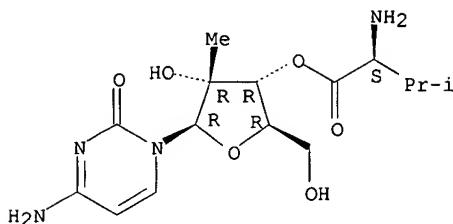
IT 640281-90-9, Valopicitabine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation of tetrahydroisoquinolinones as HDM2 ligands for the treatment of cancer)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

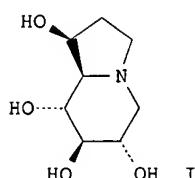


RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:894484 CAPLUS
DN 145:285094
TI Glucosidase inhibitor combinations with adjunctive therapies for treating or preventing Flaviviridae infections
IN Dugourd, Dominique; Rubinchik, Evelina; Clement, Jacob; Friedland, Hillel David
PA Migenix Inc., Can.
SO U.S. Pat. Appl. Publ., 69pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| PI US 2006194835 | A1 | 20060831 | US 2006-351885 | 20060209 |
| WO 2006096285 | A2 | 20060914 | WO 2006-US4927 | 20060209 |
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KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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| PRAI US 2005-651910P | P | 20050209 | | |
| US 2005-664297P | P | 20050321 | | |
| US 2005-735464P | P | 20051112 | | |

GI

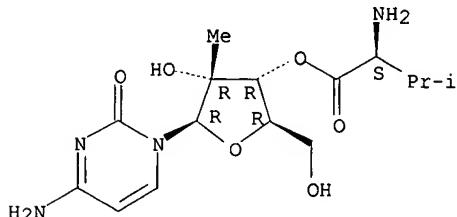


AB The present disclosure relates generally to compns. having a glucosidase inhibitor [castanospermine (I) or a derivative thereof, such as celgosivir] in combination with adjunctive therapies of compds. that alter immune function (such as interferon) and compds. that alter viral replication (such as nucleoside analogs like ribavirin), which can be used to treat or prevent infections caused by or associated with a virus of the Flaviviridae family, particularly infections caused by or associated with Hepatitis C virus (HCV). Examples include synergy of castanospermine or celgosivir in combination with other drugs such as interferons in a checkboard approach.
IT 640725-71-9, NM283
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(glucosidase inhibitor combinations with adjunctive therapies for treating or preventing Flaviviridae infections)

RN 640725-71-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, dihydrochloride (9CI) (CA INDEX NAME)

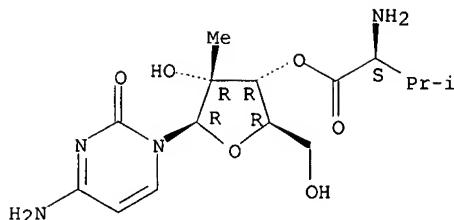
Absolute stereochemistry.



● 2 HCl

L4 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2006:425398 CAPLUS
 DN 145:39734
 TI Nucleoside analog inhibitors of hepatitis C virus replication
 AU Carroll, S. S.; Olsen, D. B.
 CS Department of Antiviral Research, Merck Research Laboratories, West Point, PA, 19486, USA
 SO Infectious Disorders: Drug Targets (2006), 6(1), 17-29
 CODEN: IDDTAD; ISSN: 1871-5265
 PB Bentham Science Publishers Ltd.
 DT Journal; General Review
 LA English
 AB A review. Of the 30 compds. currently marketed in the United States for treatment of viral infections, 15 are nucleoside analogs, demonstrating the utility of this class of compound as a source of antiviral drugs. The success of nucleoside analogs in treating other viral infections provides a compelling rationale for the significant effort that is currently being devoted to the discovery and development of nucleoside analogs to treat infection by hepatitis C virus (HCV) that may lead to improvements in response rates compared to currently available therapies. Several different approaches were adopted to identify promising analogs, including the use of surrogate viruses in cell culture assays, screening in the cell-based bicistronic HCV replicon assay, and screening nucleoside triphosphates for the ability to inhibit the activity of the HCV RNA-dependent RNA polymerase in vitro. Several classes of ribonucleoside analogs with modifications of the ribose inhibit HCV replication. Nucleoside analogs incorporating a 2'-C-Me modification are potent inhibitors in the replicon assay in the absence of cytotoxicity, and appear to exert their inhibition by acting as functional chain terminators of RNA synthesis. NM283, a prodrug of 2'-C-methylcytidine, has entered clin. trials and demonstrated viral load redns. in subjects infected with genotype 1 HCV, a genotype known to be difficult to treat effectively with currently approved therapies. Overall, results to date offer encouragement that improved therapies to treat HCV infection including newly developed nucleoside analogs may become available within the next few years.
 IT 640725-71-9, NM 283
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (nucleoside analog inhibitors of hepatitis C virus replication)
 RN 640725-71-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



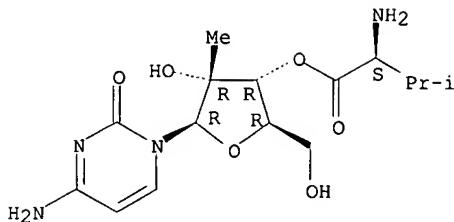
● 2 HCl

RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2006:342840 CAPLUS
 DN 144:381956
 TI Combination antiviral compositions comprising castanospermine and use for the treatment and prevention of infections caused by or associated with a virus of the Flaviviridae family
 IN Dugourd, Dominique
 PA Migenix Inc., Can.
 SO PCT Int. Appl., 54 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ,
NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,
YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM | | | | |
| US 2006093577 | A1 | 20060504 | US 2005-244811 | 20051006 |
| PRAI US 2004-616787P | P | 20041006 | | |
| AB The invention discloses the use of castanospermine in combination with another therapeutic agent to treat or prevent infections caused by or associated with a virus of the Flaviviridae family, particularly infections caused by or associated with Hepatitis C virus (HCV), and to the use of such compds. to examine the biol. mechanisms of HCV infection. | | | | |
| IT 882489-96-5 | | | | |
| RL: BSU (Biological study, unclassified); BIOL (Biological study)
(castanospermine-containing combination antiviral compns., and use for treatment of Flaviviridae infections) | | | | |
| RN 882489-96-5 CAPLUS | | | | |
| CN L-Valine, 3'-ester with 2'-C-methylcytidine, mixt. with (1S,6S,7R,8R,8aR)-octahydro-1,6,7,8-indolizinetetrol (9CI) (CA INDEX NAME) | | | | |
| CM 1 | | | | |
| CRN 640281-90-9 | | | | |
| CMF C15 H24 N4 O6 | | | | |

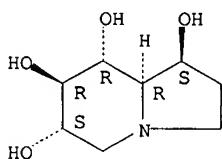
Absolute stereochemistry.



CM 2

CRN 79831-76-8
CMF C8 H15 N O4

Absolute stereochemistry. Rotation (+).

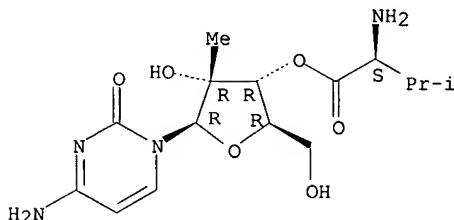


IT 640281-90-9, Valopicitabine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (castanospermine-containing combination antiviral compns., and use for
 treatment of Flaviviridae infections)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2006:149315 CAPLUS
 DN 144:205728
 TI Methods using a Type II interferon receptor agonist alone or in
 combination with a direct antiviral drug for treating hepatitis C virus
 infection

IN Blatt, Lawrence M.
 PA Intermune, Inc., USA
 SO PCT Int. Appl., 139 pp.
 CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|-------|----------|-----------------|----------|
| ----- | ----- | ----- | ----- | ----- |
| PI WO 2006016930 | A2 | 20060216 | WO 2005-US16927 | 20050513 |
| WO 2006016930 | A3 | 20060803 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, | | | | |

NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
 SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
 ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF,
 CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM,
 KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG,
 KZ, MD, RU, TJ, TM

PRAI US 2004-571322P P 20040514

AB The invention provides methods for treating hepatitis C virus (HCV) infection; methods for reducing the incidence of complications associated with HCV and cirrhosis of the liver; and methods for reducing viral load, or reducing the time to viral clearance, or reducing morbidity or mortality in the clin. outcomes, in patients suffering from HCV infection. The methods generally involve administering to the individual a Type II interferon receptor agonist alone or in combination with a direct antiviral drug.

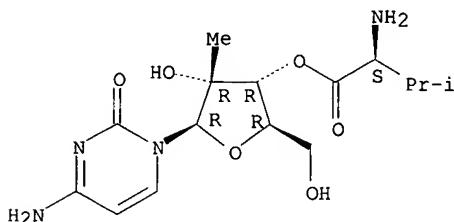
IT 640725-71-9, NM 283

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (type II interferon receptor agonist alone or in combination with direct antiviral drug for treating hepatitis C virus infection)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, dihydrochloride (9CI) (CA INDEX NAME)

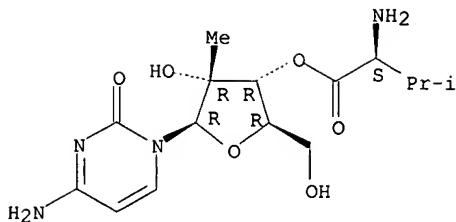
Absolute stereochemistry.



● 2 HCl

L4 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2005:1151389 CAPLUS
 DN 145:271979
 TI NM 283, an efficient prodrug of the potent anti-HCV agent 2'-C-methylcytidine
 AU Pierra, C.; Benzaria, S.; Amador, A.; Moussa, A.; Mathieu, S.; Storer, R.; Gosselin, G.
 CS Laboratoire Cooperatif Idenix, CNRS, Universite Montpellier II, Montpellier, 5, Fr.
 SO Nucleosides, Nucleotides & Nucleic Acids (2005), 24(5-7), 767-770
 CODEN: NNNAFY; ISSN: 1525-7770
 PB Taylor & Francis, Inc.
 DT Journal
 LA English
 OS CASREACT 145:271979
 AB In order to improve the oral bioavailability of 2'-C-methylcytidine, a potent anti-HCV agent, the corresponding 3'-O-L-valinyl ester derivative (NM 283) has been synthesized. Based on its ease of synthesis and its physicochem. properties, NM 283 has emerged as a promising antiviral drug for treatment of chronic HCV infection.
 IT 640725-71-9P
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prodrug; preparation of NM 283 as efficient prodrug of potent anti-HCV agent 2'-C-methylcytidine)
 RN 640725-71-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

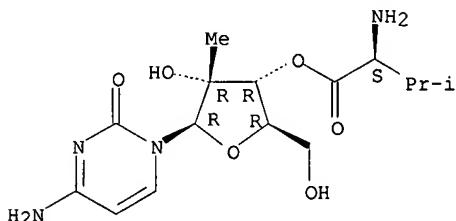


● 2 HCl

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:684531 CAPLUS
DN 143:431740
TI Emerging drugs for chronic hepatitis C
AU Bhopale, Girish Mahadeorao; Nanda, Rabindra Kumar
CS Research and Development Division, Hindustan Antibiotics Limited, Pimpri,
Pune, 411018, India
SO Hepatology Research (2008), 32(3), 146-153
CODEN: HPRSFH; ISSN: 1086-6346
PB Elsevier B.V.
DT Journal; General Review
LA English
AB A review. Hepatitis C virus (HCV) is a major cause of chronic hepatitis, liver cirrhosis and hepatocellular carcinoma worldwide. A combination therapy comprising pegylated interferon and ribavirin currently represents the most effective therapy for chronic HCV infection. The limitations of this current therapy mainly its efficacy and significant side effects have prompted the development of new drugs. Few categories of therapeutic agents appear promising for future therapy, e.g. novel interferons, ribavirin analogs, antisense oligonucleotides, short interfering RNAs, ribozymes, enzyme inhibitors, immunomodulatory agents, antifibrotic agents, therapeutic vaccines and antibodies. Few drugs belong to afore-mentioned categories have already reached the different clin. phases of development. The present article highlights the status of current available therapies and emerging drugs for the treatment of hepatitis C.
IT 640725-71-9, NM 283
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(NM283 proved promising therapeutic effect in treating chronic
hepatitis C patient)
RN 640725-71-9 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, dihydrochloride (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



● 2 HCl

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/607,909

L4 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:216597 CAPLUS
DN 142:291323
TI Compositions and methods for the treatment of severe acute respiratory syndrome (SARS)
IN Hardee, Greg; Dellamary, Luis
PA Isis Pharmaceuticals, Inc., USA
SO PCT Int. Appl. / 217 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| PI WO 2005020885 | A2 | 20050310 | WO 2004-US16196 | 20040521 |
| WO 2005020885 | A3 | 20050804 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG | | | | |

PRAI US 2003-472774P P 20030521

AB The invention provides compns. and methods for treating a coronavirus infection, especially a SARS Cov infection. The compns. comprise an antiviral nucleoside or mimetic thereof, or an antiviral antisense agent, in a form suitable for pulmonary or nasal delivery. The methods comprise administration to a patient in need thereof the effective amount of an antiviral composition by pulmonary or nasal instillation.

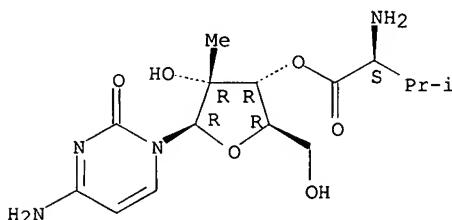
IT 640281-90-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for treatment of severe acute respiratory syndrome)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:515518 CAPLUS
DN 141:38814
TI Process for the production of 2'-branched nucleosides
IN Storer, Richard; Moussa, Adel; Chaudhuri, Narayan; Waligora, Frank
PA Idenix Cayman Limited, Cayman I.
SO PCT Int. Appl. / 90 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 4

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| PI WO 2004052899 | A2 | 20040624 | WO 2003-US39643 | 20031212 |
| WO 2004052899 | A3 | 20050331 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, | | | | |

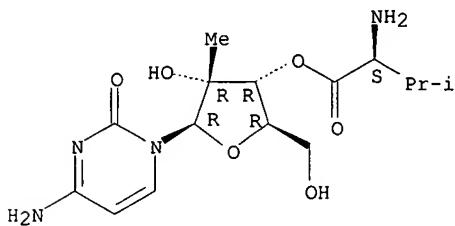
McIntosh

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
 NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
 TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
 BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
 TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2509687 AA 20040624 CA 2003-2509687 20031212
 AU 2003300901 A1 20040630 AU 2003-300901 20031212
 US 2005020825 A1 20050127 US 2003-735408 20031212
 EP 1585529 A2 20051019 EP 2003-812993 20031212
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 CN 1744903 A 20060308 CN 2003-80109576 20031212
 JP 2006514993 T2 20060518 JP 2005-511773 20031212
 NO 2005003115 A 20050818 NO 2005-3115 20050624
 PRAI US 2002-432766P P 20021212
 US 2003-466194P P 20030428
 WO 2003-US39643 W 20031212
 OS CASREACT 141:38814
 GI



- AB The present invention provides an improved process for preparing ss-D and ss-L 2'-C-methyl-nucleosides and 2'-C-methyl-3'-O-ester nucleosides, e.g. I, via glycosylation of methylribonolactone with nucleobases.
- IT 640725-71-9P
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 (process for production of 2'-branched nucleosides via glycosylation of methylribonolactone with nucleobases)
- RN 640725-71-9 CAPLUS
- CN L-Valine, 3'-ester with 2'-C-methylcytidine, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 2 HCl

L4 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2004:453348 CAPLUS
 DN 141:17578

10/607,909

TI Treatment of Flaviviridae infection with 2'-branched nucleosides and another mutation-inducing drug such as interferon
IN Sommadossi, Jean-Pierre; La Colla, Paolo; Standring, David; Bichko, Vadim;
PA Idenix (Cayman) Limited, Cayman I.; Universita Degli Studi Di Cagliari
SO PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------|
| WO 2004046331 | A2 | 20040603 | WO 2003-US36714 | 20031117 |
| WO 2004046331 | A3 | 20060302 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2506129 | AA | 20040603 | CA 2003-2506129 | 20031117 |
| AU 2003298658 | A1 | 20040615 | AU 2003-298658 | 20031117 |
| US 2005031588 | A1 | 20050210 | US 2003-715729 | 20031117 |
| EP 1576138 | A2 | 20050921 | EP 2003-796412 | 20031117 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003016363 | A | 20051004 | BR 2003-16363 | 20031117 |
| JP 2006519753 | T2 | 20060831 | JP 2004-553823 | 20031117 |
| CN 1849142 | A | 20061018 | CN 2003-80108747 | 20031117 |
| NO 2005002920 | A | 20050815 | NO 2005-2920 | 20050615 |

PRAI US 2002-426675P P 20021115
WO 2003-US36714 W 20031117

OS MARPAT 141:17578

AB The present invention discloses a method for the treatment of Flaviviridae infection that includes the administration of a 2'-branched nucleoside, or a pharmaceutically acceptable prodrug and/or salt thereof, to a human in need of therapy in combination or alternation with a drug that directly or indirectly induces a mutation in the viral genome at a location other than a mutation of a nucleotide that results in a change from serine to a different amino acid in the highly conserved consensus sequence, XRXSGXXXT, of domain B of the RNA polymerase region, or is associated with such a mutation. The invention also includes a method to detect a mutant strain of Flaviviridae and a method for its treatment. Thus, in bovine viral diarrhea virus (BVDV)-infected MDBK cells treated with β-D-2'-methylcytidine, viruses resistant to the nucleoside appeared. The drug resistance was associated with a mutation in the NS5B gene which resulted in an S405T substitution in the encoded RNA-dependent RNA polymerase. These mutant viruses were sensitive to Intron A (interferon α-2b). Intron A and β-D-2'-methylcytidine exhibited synergistic inhibitory activity on BVDV growth in MDBK cells.

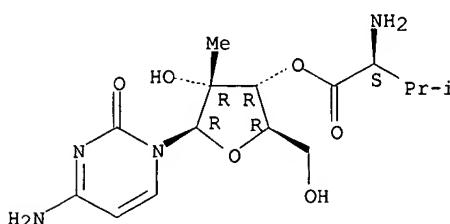
IT 640281-90-9

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of Flaviviridae infection with 2'-branched nucleosides and another mutation-inducing drug such as interferon)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



checked
ODL

McIntosh

L4 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2004:20697 CAPLUS
 DN 140:87662
 TI 2'- and 3'-nucleoside prodrugs for treating Flaviviridae infections
 IN Sommadossi, Jean-pierre; La Colla, Paolo; Storer, Richard; Gosselin, Gilles
 PA Idenix (Cayman) Limited, Cayman I.; Centre National de la Recherche Scientifique; Universita Degli Studi di Cagliari
 SO PCT Int. Appl., 2498 pp.
 CODEN: PIXXD2

DT Patent
 LA English
 FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2004003000 | A2 | 20040108 | WO 2003-IB3901 | 20030627 |
| | WO 2004003000 | A3 | 20041104 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2490200 | AA | 20040108 | CA 2003-2490200 | 20030627 |
| | AU 2003263412 | A1 | 20040119 | AU 2003-263412 | 20030627 |
| | EP 1525209 | A2 | 20050427 | EP 2003-761749 | 20030627 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | CN 1678621 | A | 20051005 | CN 2003-820690 | 20030627 |
| | JP 2005537242 | T2 | 20051208 | JP 2004-517162 | 20030627 |
| | CN 1761677 | A | 20060419 | CN 2003-820501 | 20030627 |
| | WO 2005020884 | A2 | 20050310 | WO 2004-US15395 | 20040514 |
| | WO 2005020884 | A3 | 20060622 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1656093 | A2 | 20060517 | EP 2004-776022 | 20040514 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| | NO 2005000466 | A | 20050323 | NO 2005-466 | 20050127 |
| PRAI | US 2002-392350P | P | 20020628 | | |
| | US 2002-392351P | P | 20020628 | | |
| | US 2003-466194P | P | 20030428 | | |
| | US 2003-470949P | P | 20030514 | | |
| | WO 2003-IB3901 | W | 20030627 | | |
| | WO 2004-US15395 | W | 20040514 | | |

OS MARPAT 140:87662
 AB 2' And 3'-Prodrugs of 1'-, 2'-, 3'-, or 4'-branched β -D or β -L nucleosides, or their pharmaceutically acceptable salts and derivs., are described which are useful in the prevention and treatment of Flaviviridae infections and other related conditions. These modified nucleosides provide superior results against flaviviruses and pestiviruses, including hepatitis C virus and viruses generally that replicate through an RNA-dependent RNA reverse transcriptase. Compds., compns., methods and uses are provided for the treatment of Flaviviridae infection, including HCV infection, that include the administration of an effective amount of the prodrugs of the invention, or their pharmaceutically acceptable salts or derivs. These drugs may optionally be administered in combination or alternation with further antiviral agents to prevent or treat Flaviviridae infections and other related conditions. Preparation of compds. of the invention is included.

IT 640725-71-9P

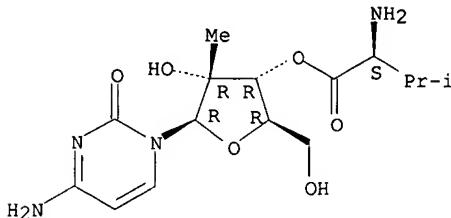
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(nucleoside prodrugs for treating Flaviviridae infections)

RN 640725-71-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

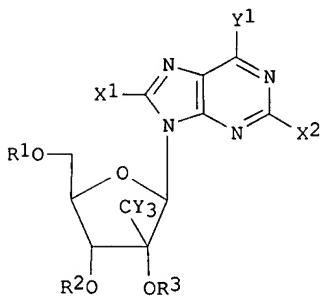


●2 HCl

L4 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2004:20696 CAPLUS
 DN 140:77365
 TI Preparation of modified 2'- and 3'-nucleoside prodrugs for treating Flaviviridae infections
 IN Sommadossi, Jean-pierre; La Colla, Paolo; Storer, Richard; Gosselin, Gilles
 PA Idenix-(Cayman)-Limited, Cayman I.; Universita degli studi di Cagliari; Centre National de la Recherche Scientifique
 SO PCT Int. Appl., 201 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 4

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2004002999 | A2 | 20040108 | WO 2003-IB3246 | 20030627 |
| WO 2004002999 | A3 | 20040812 | | |
| WO 2004002999 | C1 | 20050217 | | |
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| CA 2490191 | AA | 20040108 | CA 2003-2490191 | 20030627 |
| AU 2003247084 | A1 | 20040119 | AU 2003-247084 | 20030627 |
| EP 1523489 | A2 | 20050420 | EP 2003-761744 | 20030627 |
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| CN 1678621 | A | 20051005 | CN 2003-820690 | 20030627 |
| JP 2005533817 | T2 | 20051110 | JP 2004-517158 | 20030627 |
| CN 1761677 | A | 20060419 | CN 2003-820501 | 20030627 |
| WO 2005020884 | A2 | 20050310 | WO 2004-US15395 | 20040514 |
| WO 2005020884 | A3 | 20060622 | | |
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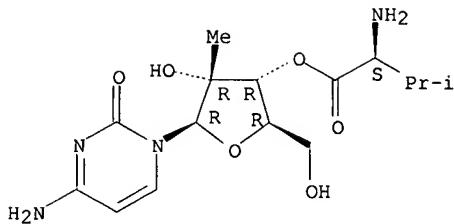
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG
 EP 1656093 A2 20060517 EP 2004-776022 20040514
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 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
 NO 2005000465 A 20050127 NO 2005-465 20050127
 PRAI US 2002-392350P P 20020628 ✓
 US 2002-392351P P 20020628 ✓
 US 2003-466194P P 20030428
 US 2003-470949P P 20030514
 WO 2003-IB3246 W 20030627
 WO 2004-US15395 W 20040514
 OS MARPAT 140:77365
 GI



AB 2' And/or 3' prodrugs of 1', 2', 3' or 4'-branched-nucleosides I, wherein R1-R3 are independently H, phosphate, alkyl, acyl, CO-alkyl, CO-aryl, CO-alkoxyalkyl, CO-aryloxyalkyl, CO-substituted aryl, sulfonate ester, benzyl, wherein the Ph group is optionally substituted with one or more substituents, alkylsulfonyl, arylsulfonyl, aralkylsulfonyl, lipid, amino acid, carbohydrate, peptide, cholesterol; Y1 is hydrogen, bromo, chloro, fluoro, iodo, CN, OH, OR4, NH2, NHR4, NR4R5, SH or SR4; X1 and X2 are independently alkyl, CH3, CF3, CY3, 2-Br-Et, CH2F, CH2Cl, CH2CF3, CF2CF3, CY2CY3, CH2OH, alkenyl, alkynyl, COOH, COOR4, COO-alkyl, COO-aryl, CO-O-alkoxyalkyl, CONH2, CONHR4, CON(R4)2, halo, CN, N3, OH, OR4, NH2, NHR4, NR4R5, SH or SR5; Y is independently H, halo; and each R4 and R5 is independently hydrogen, acyl, alkyl, lower alkyl, alkenyl, alkynyl or cycloalkyl, and their pharmaceutically acceptable salts and derivs. are described. These prodrugs are useful in the prevention and treatment of Flaviviridae infections, including HCV infection, and other related conditions. Compds. and compns. of the prodrugs of the present invention are described. Methods and uses are also provided that include the administration of an effective amount of the prodrugs of the present invention, or their pharmaceutically acceptable salts or derivs. These drugs may optionally be administered in combination or alteration with further anti-viral agents to prevent or treat Flaviviridae infections and other related conditions. Thus, antiviral activity of β-D-2'-C-methyl-7-methyl-6-phenyl-3a,5,8a-tetrahydro-1,3,4,5,7a-penta-aza-s-indacen-8-one is reported.

IT 640281-90-9P
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of modified and nucleoside prodrugs for treating flaviviridae infections).
 RN 640281-90-9 CAPLUS
 CN L-Valine, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
 AN 2004:20443 CAPLUS
 DN 140:70984
 TI 2'-C-methyl-3'-O-L-valine ester ribofuranosyl cytidine for treatment of flaviviridae infections
 IN Sommadossi, Jean-Pierre; La Colla, Paolo
 PA Idenix (Cayman) Limited, Cayman I.; Universita Degli Studi di Cagliari
 SO PCT Int. Appl., 110 pp.

CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 4

M/ app.

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|------------|-----------------|----------|
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| | WO 2004002422 | A3 | 20050407 | | |
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| CA | 2489552 | AA | 20040108 | CA 2003-2489552 | 20030627 |
| AU | 2003248748 | A1 | 20040119 | AU 2003-248748 | 20030627 |
| US | 2004077587 ✓ | A1 | 20040422 | US 2003-607909 | 20030627 |
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| CN | 1678326 | A | 20051005 | CN 2003-820701 | 20030627 |
| JP | 2005533824 | T2 | 20051110 | JP 2004-518041 | 20030627 |
| WO | 2005020884 | A2 | 20050310 | WO 2004-US15395 | 20040514 |
| WO | 2005020884 | A3 | 20060622 | | |
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| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP | 1656093 | A2 | 20060517 | EP 2004-776022 | 20040514 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |
| NO | 2005000490 | A | 20050127 | NO 2005-490 | 20050127 |
| PRAI | US 2002-392351P | P | 20020628 ✓ | | |
| | US 2003-466194P | P | 20030428 | | |
| | US 2003-470949P | P | 20030514 | | |
| | WO 2003-US20431 | W | 20030627 | | |
| | WO 2004-US15395 | W | 20040514 | | |
| OS | MARPAT 140:70984 | | | | |
| AB | The 3'-L-valine ester of β-D-2'-C-methyl-ribofuranosyl cytidine provides superior results against flaviviruses and pestiviruses, including hepatitis C virus. Based on this discovery, compds., compns., methods and uses are provided for the treatment of flaviviridae, including HCV, that include the administration of an effective amount of val-mCyd or its salt, | | | | |

10/607,909

ester, prodrug or derivative, optionally in a pharmaceutically acceptable carrier. In an alternative embodiment, val-mCyd is used to treat any virus that replicates through an RNA-dependent RNA polymerase. Several examples are provided of the pharmacol., mechanism of action, metabolism, side effects, and clin. efficacy of the title compound

IT 640281-90-9D, salts 642075-50-1 642075-51-2

642075-52-3 642075-53-4 642075-54-5

642075-55-6 642075-56-7 642075-57-8

642075-58-9 642075-59-0 642075-60-3

642075-61-4 642075-62-5 642075-63-6

642075-64-7 642075-65-8 642075-66-9

642075-67-0 642075-68-1 642075-69-2

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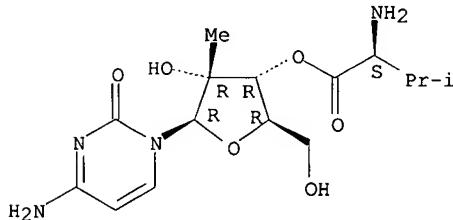
642075-77-2

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ribofuranosylcytidine methylvaline ester combined with other
antivirals for treatment of flaviviridae infections)

RN 640281-90-9 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 642075-50-1 CAPLUS

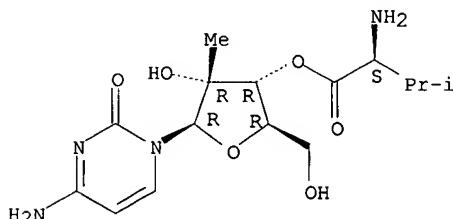
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 4-methylbenzenesulfonate
(salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9

CMF C15 H24 N4 O6

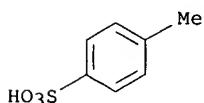
Absolute stereochemistry.



CM 2

CRN 104-15-4

CMF C7 H8 O3 S



RN 642075-51-2 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, methanesulfonate (salt) (9CI)
(CA INDEX NAME)

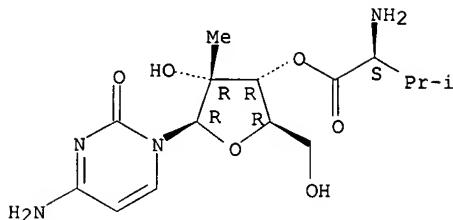
McIntosh

10/607, 909

CM 1

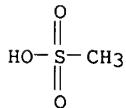
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S



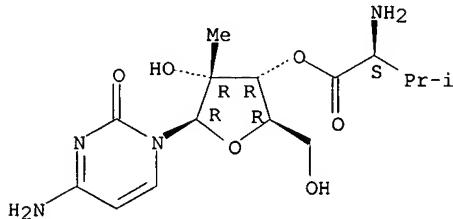
RN 642075-52-3 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, acetate (salt) (9CI) (CA INDEX NAME)

CM 1

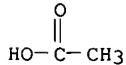
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.



CM 2

CRN 64-19-7
CMF C2 H4 O2



RN 642075-53-4 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxy-1,2,3-propanetricarboxylate (salt) (9CI) (CA INDEX NAME)

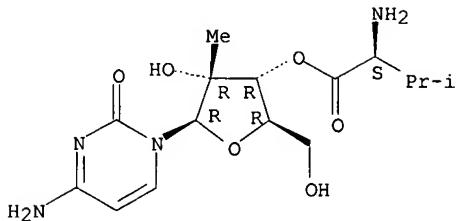
CM 1

McIntosh

10/607,909

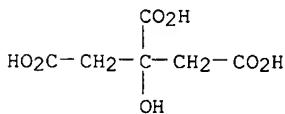
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.



CM 2

CRN 77-92-9
CMF C6 H8 O7

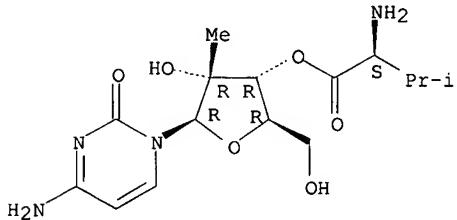


RN 642075-54-5 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, propanedioate (salt) (9CI)
(CA INDEX NAME)

CM 1

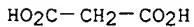
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.



CM 2

CRN 141-82-2
CMF C3 H4 O4



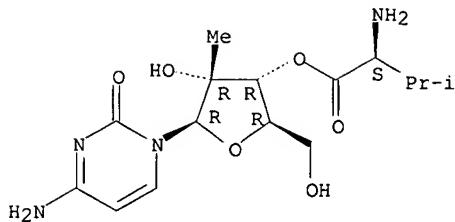
RN 642075-55-6 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2R,3R)-2,3-dihydroxybutanedioate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.

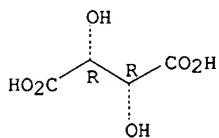
10/607, 909



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

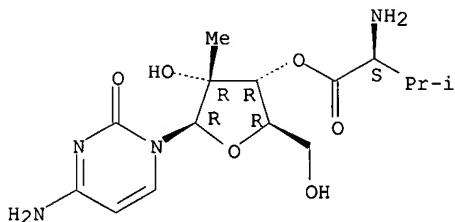


RN 642075-56-7 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, butanedioate (salt) (9CI)
(CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.



CM 2

CRN 110-15-6
CMF C4 H6 O4

HO2C—CH2—CH2—CO2H

RN 642075-57-8 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, benzoate (salt) (9CI) (CA INDEX NAME)

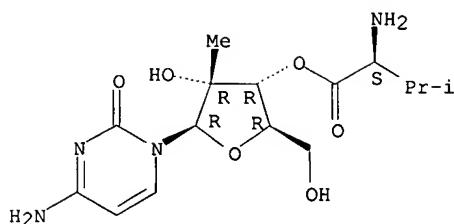
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.

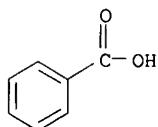
McIntosh

10/607,909



CM 2

CRN 65-85-0
CMF C7 H6 O2

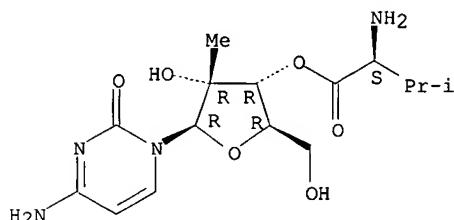


RN 642075-58-9 CAPLUS
CN L-Ascorbic acid, compd. with L-valine 3'-ester with 2'-C-methylcytidine
(9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

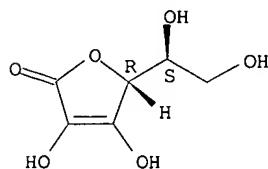
Absolute stereochemistry.



CM 2

CRN 50-81-7
CMF C6 H8 O6

Absolute stereochemistry.



RN 642075-59-0 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-oxopentanedioate (salt)
(9CI) (CA INDEX NAME)

CM 1

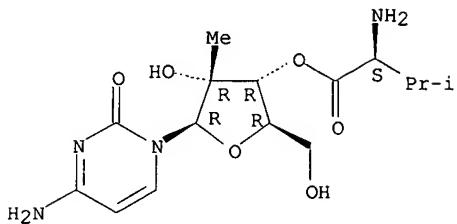
CRN 640281-90-9

McIntosh

10/607,909

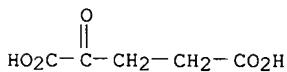
CMF C15 H24 N4 O6

Absolute stereochemistry.



CM 2

CRN 328-50-7
CMF C5 H6 O5



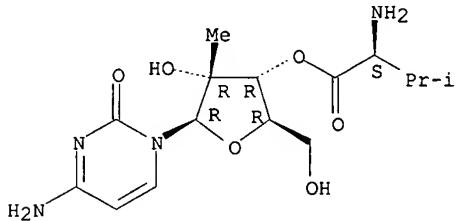
RN 642075-60-3 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2,3-dihydroxypropyl phosphate (salt) (9CI) (CA INDEX NAME)

CM 1

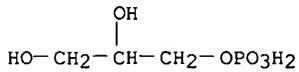
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.



CM 2

CRN 57-03-4
CMF C3 H9 O6 P



RN 642075-61-4 CAPLUS

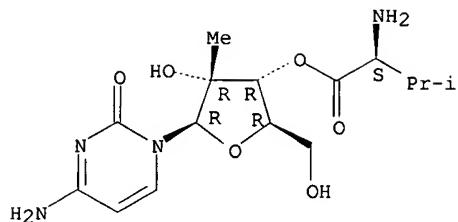
CN L-Valine, 3'-ester with 2'-C-methylcytidine, formate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.

10/607, 909



CM 2

CRN 64-18-6
CMF C H2 O2

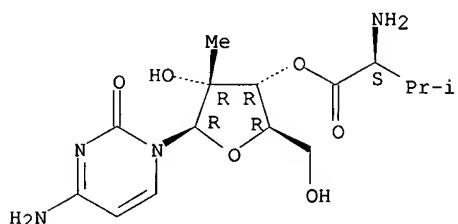
O=CH-OH

RN 642075-62-5 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2E)-2-butenedioate (salt)
(9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

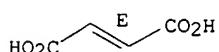
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



RN 642075-63-6 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, propanoate (salt) (9CI) (CA INDEX NAME)

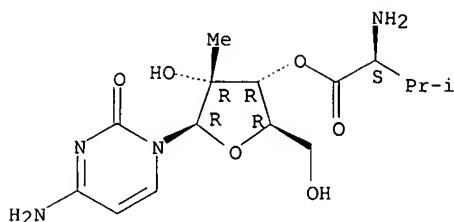
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.

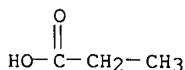
McIntosh

10/607, 909



CM 2

CRN 79-09-4
CMF C3 H6 O2



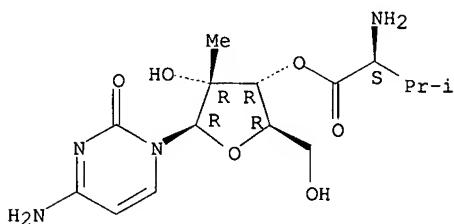
RN 642075-64-7 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydroxyacetate (salt) (9CI)
(CA INDEX NAME)

CM 1

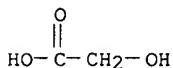
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.



CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 642075-65-8 CAPLUS

CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxypropanoate (salt)
(9CI) (CA INDEX NAME)

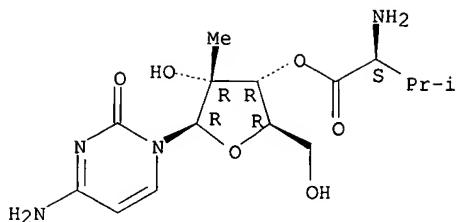
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.

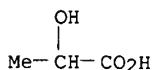
McIntosh

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CM 2

CRN 50-21-5
CMF C3 H6 O3

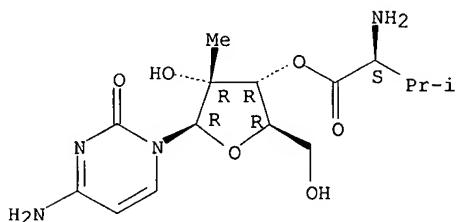


RN 642075-66-9 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-oxopropanoate (salt) (9CI)
(CA INDEX NAME)

CM 1

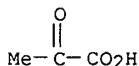
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.



CM 2

CRN 127-17-3
CMF C3 H4 O3



RN 642075-67-0 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, ethanedioate (salt) (9CI)
(CA INDEX NAME)

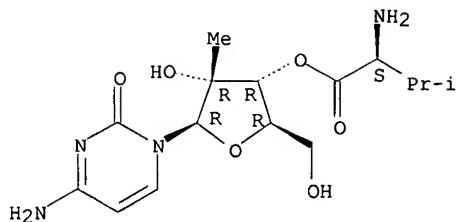
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.

McIntosh

10/607, 909



CM 2

CRN 144-62-7
CMF C2 H2 O4

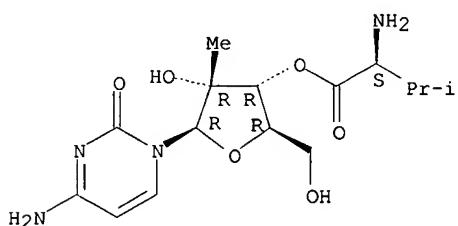


RN 642075-68-1 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, (2Z)-2-butenedioate (salt)
(9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

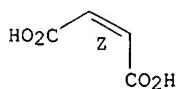
Absolute stereochemistry.



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



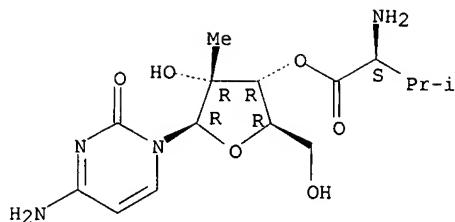
RN 642075-69-2 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, 2-hydroxybenzoate (salt)
(9CI) (CA INDEX NAME)

CM 1

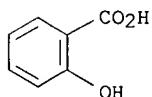
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.

McIntosh



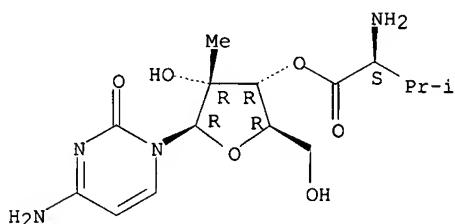
CM 2

CRN 69-72-7
CMF C7 H6 O3RN 642075-70-5 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, sulfate (salt) (9CI) (CA INDEX NAME)

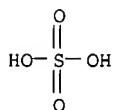
CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.



CM 2

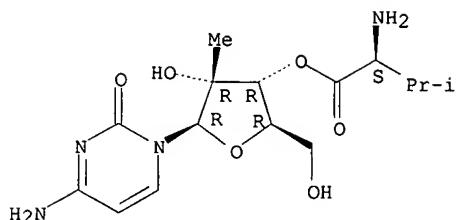
CRN 7664-93-9
CMF H2 O4 SRN 642075-71-6 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, nitrate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 640281-90-9
CMF C15 H24 N4 O6

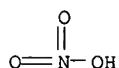
Absolute stereochemistry.

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CM 2

CRN 7697-37-2
CMF H N O3

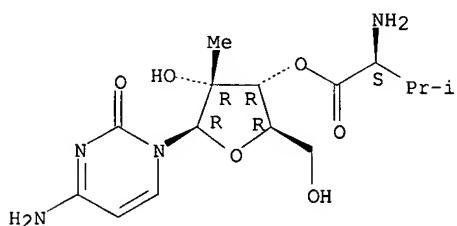


RN 642075-72-7 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, carbonate (salt) (9CI) (CA INDEX NAME)

CM 1

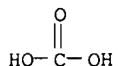
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.



CM 2

CRN 463-79-6
CMF C H2 O3

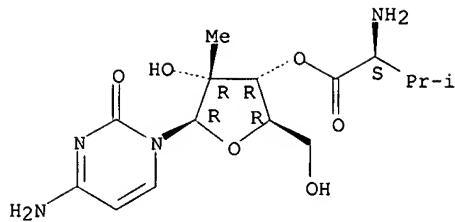


RN 642075-74-9 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydrobromide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

McIntosh

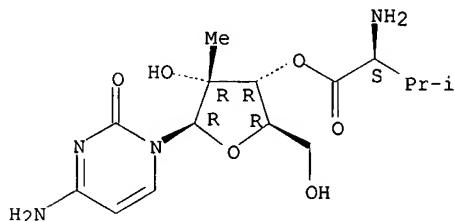
10/607, 909



●x HBr

RN 642075-75-0 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, hydriodide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



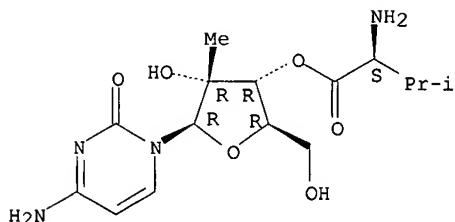
●x HI

RN 642075-76-1 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, carbonate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

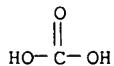
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.



CM 2

CRN 463-79-6
CMF C H2 O3



RN 642075-77-2 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, phosphate (salt) (9CI) (CA

McIntosh

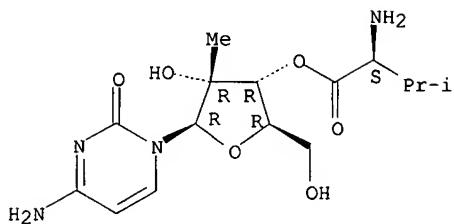
10/607,909

INDEX NAME)

CM 1

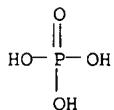
CRN 640281-90-9
CMF C15 H24 N4 O6

Absolute stereochemistry.



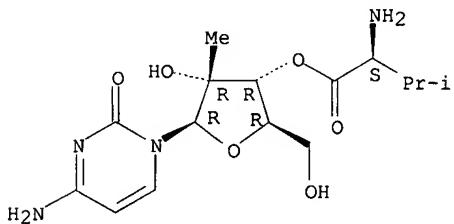
CM 2

CRN 7664-38-2
CMF H3 O4 P



IT 640281-90-9P
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ribofuranosylcytidine methylvaline ester for treatment of flaviviridae infections)
RN 640281-90-9 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine (9CI) (CA INDEX NAME)

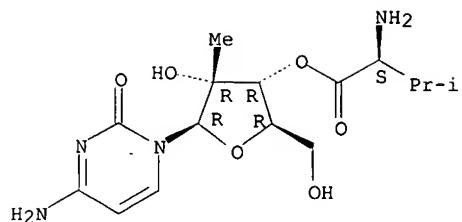
Absolute stereochemistry.



IT 640725-71-9P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ribofuranosylcytidine methylvaline ester for treatment of flaviviridae infections)
RN 640725-71-9 CAPLUS
CN L-Valine, 3'-ester with 2'-C-methylcytidine, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/607, 909



●2 HCl

=> d his

(FILE 'HOME' ENTERED AT 13:51:27 ON 08 DEC 2006)

FILE 'REGISTRY' ENTERED AT 13:51:54 ON 08 DEC 2006
L1 STRUCTURE uploaded
L2 0 S L1 SSS SAM
L3 30 S L1 FULL

FILE 'CAPLUS' ENTERED AT 13:52:32 ON 08 DEC 2006
L4 16 S L3

McIntosh